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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,123	01/18/2007	Makoto Inoue	50026/061001	7683

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CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
03/03/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,123	INOUE ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *11-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/16/07, 4/16/07, 7/16/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received

Election/Restrictions

Applicant's election with traverse of group I, claims 1-10 is acknowledged. Applicants disagree with the Office's identification of the special technical feature of the present invention. Applicants submit that the special technical feature of the present invention is "making a modified virus using an alternative protease than the protease which cleaves the wild-type protein, where propagation of the produced viral vector does not depend on the alternative protease." Applicants emphasize that in the present method the modified viral protein is cleaved but does not comprise a gene encoding the modified viral protein. The Office agrees with Applicant's arguments. However, the Office cites another reference that does disclose the special technical feature of the present invention. Heminway et al. (Virus Research, 1995, Vol. 36, p. 15-35) disclose a method of producing a Sendai virus using an alternative protease than the protease which cleaves the wild-type protein, where propagation of the produced viral vector does not depend on the alternative protease, wherein the modified viral protein is cleaved but does not comprise a gene encoding the modified viral protein. Heminway et al. disclose a Sendai virus vector comprising an alternative protease (see the entire document).

Thus because Heminway et al. disclose the special technical feature of the present invention the claims lack unity of invention and the restriction is set forth as it applies to U.S. practice. The restriction requirement is deemed proper and is made FINAL.

Claims 11-35 are withdrawn because they are drawn to the non-elected invention. Claims 1-10 are under examination.

Priority

Acknowledgment is made for priority to a PCT/JP05/00708 and Japanese document 2004-014654. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 2/16/2007, 4/16/2007, and 7/16, 2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for amino acid sequence set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason (s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The sequences recited in claims 6, 7, 17, 18, 31, and 32 have at least 4 amino acids. The sequence rules embrace all amino acid sequences of at least 4 amino acids. See MPEP 2421.02

> The sequence rules embrace all unbranched nucleotide sequences with ten or more bases and all unbranched, non-D amino acid sequences with four or more amino acids, provided that there are at least 4 "specifically defined" nucleotides or amino acids. The rules apply to all sequences in a given application, whether claimed or not. All such sequences are relevant for the purposes of building a comprehensive database and properly assessing prior art. It is therefore essential that all sequences, whether only disclosed or also claimed, be included in the database.

The time for response to this Notice to Comply is the same as the time for response to the present Office action, which is 3 months from mailing of this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims lack a measurement step or positive process steps to carry out the claimed methods. In the instant case, the claims fail to recite the steps necessary to carry out the method of producing a virus whose propagation depends on cleavage of a viral protein by protease. While the components of the virus are recited in the claims, there is lack of recitation of the steps required to propagate the virus.

While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The minimum requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized, and a correlation step describing how the results of the assay allow for the determination.

Additionally, claim 1 recites: "(…) the alternative protease wherein the produced virus comprises the modified viral protein that is cleaved but does not comprise a gene encoding the modified viral protein." This recitation is ambiguous, it is not clear how the produced virus can comprise the modified viral protein that is cleaved and at the same time do not comprise a gene encoding the modified viral protein. Additionally the recitation of "alternative" proteases does

not set metes and bounds for the claimed proteases. The present specification does not provide a definition for the meaning of an "alternative" protease. Clarification and correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims are broadly drawn to a method for producing a virus whose propagation depends on cleavage of a viral protein by protease wherein the method comprises the step of producing the virus in the presence of (i) a modified viral protein in which a cleavage sequence for the protease is changed to cleavage sequence for an alternative protease and (ii) the alternative protease wherein the produced virus comprises the modified viral protein that is cleaved but does not comprise a gene encoding the modified viral protein.

The claims are rejected because the present specification lack an adequate written description for **1)** the genus of the claimed modified viral proteins, **2)** the genus of the cleavage sequence for an alternative protease, **3)** the genus of alternative proteases, and **4)** the genus of the modified viral proteins that are cleaved but do not comprise a gene encoding the modified viral protein.

The claimed modified viral proteins broadly encompass many different types of modifications, which could be amino acid substitutions, deletions, addition of sugar and other molecules. The present specification does not provide a definition with regard to the claimed genus of the modified viral proteins. The specification does not describe what types of modifications are permissible for the virus to successfully replicate and propagate. It is noted that the claims broadly encompass any viral protein. The claimed cleavage sequence of an alternative protease broadly encompasses any alternative protease sequence, while the specification discloses an alternative protease sequence comprising Arg-Xaa-Lys/Arg-Arg and Arg-Arg-Arg-Arg. The specification does not provide an adequate written description for the large genus of alternative protease sequence. The claims do not recite a particular function that must be associated with the claimed sequences. Thus the claims lack a structure and function correlation for the claimed alternative protease sequences. The claims broadly recite "alternative proteases" that encompass a large genus of proteases. The skilled artisan would be unable to determine what specific alternative proteases could be useful in the present method. The claims broadly encompass any gene encoding the modified viral protein. There is lack of an adequate written description for the claimed genus of genes encoding the modified viral protein.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the claims broadly encompass any modifications and any alternative proteases, without identifying any specific modifications or

any specific alternative proteases, for which there is lack of support in the present specification. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of modified viral proteins or alternative proteases. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological or pharmacological activities. It is known in the art that the substitution of some amino acids within the protein sequence may cause the loss of function of the protein. See the following publications that support this unpredictability (Baker et al., Protein Structure Prediction and Structural Genomics, Science (2001) Vol. 294, No. 5540, pages 93- 96; Attwood, T. The Babel of Bioinformatics, Science (2000) Vol. 290, no. 5491, pages 471-473).

The skilled artisan cannot envision the detailed structure of a genus of modified viral proteins and alternative proteases that are contemplated in the invention. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 rejected under 35 U.S.C. 102() as being anticipated by Heminway et al. (Virus Research, 1995, Vol. 36, p. 15-35).

Claims are broadly drawn to a method for producing a virus whose propagation depends on cleavage of a viral protein by protease wherein the method comprises the step of producing the virus in the presence of (i) a modified viral protein in which a cleavage sequence for the protease is changed to cleavage sequence for an alternative protease and (ii) the alternative protease wherein the produced virus comprises the modified viral protein that is cleaved but does not comprise a gene encoding the modified viral protein. The alternative protease is furin and the alternative protease comprises Arg-Xaa-Lys/Arg-Arg and Arg-Arg-Arg-Arg. The virus is a Sendai virus. For the purposes of the present rejection it is interpreted that the slash "/" indicates that the amino acid number 3 of the present sequence is either Lys or Arg.

Heminway et al. disclose a method of producing a Sendai virus using an alternative protease than the protease which cleaves the wild-type protein (see the entire document). Heminway et al. discloses furin as the alternative protease which sequence comprises Arg-Xaa-Lys/Arg-Arg and Arg-Arg-Arg-Arg. It is noted that Heminway et al. discloses the alternative protease sequence as Arg-Xxx-Arg/Lys-Arg (see page 16). Because Xxx and Xaa could be any amino acid and because Arg at position 3 could be Lys, it is understood that Heminway et al. discloses Arg-Xaa-Lys/Arg-Arg and Arg-Arg-Arg-Arg of the present invention.

Thus by this disclosure Heminway et al. anticipate the present claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen, Ph.D./
Examiner, Art Unit 1648

/Stacy B Chen/

Primary Examiner, Art Unit 1648